Quantifying mechanical heterogeneity in microbead cell expansion using individual-cell based models

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ABSTRACT

Directing growth and cell fate for *in vitro* cell expansion requires not only fine control of biochemical factors - e.g. growth factors, oxygen, nutrients - but also the mechanical aspects of the microenvironment [1,2,3]. In microcarrier cell culture, cells are seeded on spherical polymer microbeads and proliferate until confluency. Subsequently, these beads can be clustered, resulting in large, three-dimensional aggregates of cells. How the physical properties of the bead and the characteristics of the cell culture system affect the mechanical microenvironment is still poorly understood. Moreover, measuring mechanical forces in these living aggregates is currently still not feasible. Therefore, we constructed an individual-cell based model (IBM) that describes how mechanical forces change throughout exponential cell growth on spherical microbeads.

We use a lattice-free IBM, which considers cells as elastic, deformable spherical particles [4]. At each time point, the displacements of the cells are calculated from the equation of motion, which is derived for cells that move in a low-Reynolds environment. Cell-cell contacts and cell-microbead contacts are described by the Johnson-Kendall-Roberts (JKR) potential. Simulations reveal that the adhesion energy of the bead – affected by adhesive chemical coatings – is an important determinant of the heterogeneity in mechanical stress on the cells (Figure). In general, a proof of principle is given that purely geometric and mechanical effects of cell expansion itself are sufficient to result in a large heterogeneity in mechanical stresses.

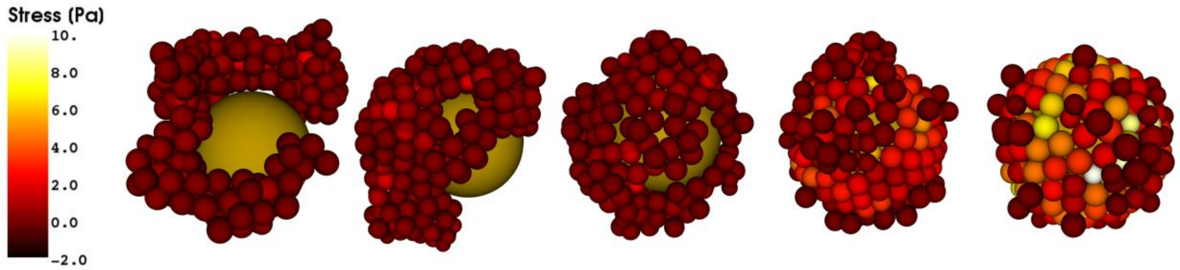

Figure: Average stress levels on cells for different cell-bead adhesion (K_a) strengths. From left to right: K_a = 2.5e-6, 5e-6, 10e-6, 20e-6 and 40e-6 J/m^2.

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